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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/843,150	04/27/2001	Pierre Chambon	065691/0219	7311

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EXAMINER	
LEFFERS JR, GERALD G	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/843,150	CHAMBON ET AL.	
	Examiner	Art Unit	
	Gerald G Leffers Jr., PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,6,8-13,15-24,26-46 and 49-54* is/are pending in the application.

4a) Of the above claim(s) *26-46 and 49-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,6,8-13,15-24,53 and 54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application on 11/29/2004 and after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on 10/28/2004 has been entered.

Response to Amendment

In the response filed on 10/28/2004, claims were amended (claims 1 & 54) and claims were cancelled (claims 2-4). Claims 1, 5-6, 8-13, 15-24, 26-46 & 49-54 are pending in the instant application, with claims 26-46 & 49-52 withdrawn from consideration as being directed to nonelected inventions. Thus, claims 1, 5-6, 8-13, 15-24 & 53-54 are under consideration in the instant office action.

With regard to pending claim 1, it is noted that the examiner has not previously rejected the embodiment recited in the amended claim as being anticipated by the art of record (i.e. Wild et al). Upon further consideration, an inherency argument is proper with regard to the amended claim and is explained in detail below. Amendment of the base claim to include the limitation of claim 16, where at least the sequences A and/or B are transcribed and translated to produce at least one protein, would obviate the inherency argument.

With regard to rejoinder of dependent process claims, applicants again request rejoinder of dependent claims once the base product claims under consideration are determined to be allowable.

Where applicant elects claims directed to the product, and a product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claims will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier.** Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. ***Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined.*** See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. ***Failure to do so may result in a loss of the right to rejoinder.***

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

It is noted that even if the currently amended claim 1 were allowable, the methods claims dependent upon claim 1 are not commensurate in scope to claim 1 as they are currently written. For example, claim 33, step (ii) recites, "inversion of sequence A and B or sequence A or sequence B." Given the configuration of SSRTS, sequence A and sequence B in currently pending claim 1, there is no way in which one could have inversion of one of sequence A or sequence B without inversion of the other sequence, as is currently recited in withdrawn claim 33. If applicants wish the withdrawn methods claims rejoined with any allowed product claim, the methods claims will have to be amended to be commensurate in scope to the product claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejected claims are directed to an isolated DNA molecule comprising two different site specific recombinase targeting sequences (SSRTS L1 & L2) flanking sequence A and sequence B in the order of 5'-L1-L2-sequence A-sequence B-L1-L2-3'. The two L1 sequences are in opposite orientation to one another. Sequences A and B can be in the same or opposite orientation. The two L2 sequences are in opposite orientation to one another. L1 and L2 are not

capable of recombination with one another. Sequences A & B can be obtained from nontranscribed sequences or from transcribed but untranslated sequences.

Claims 1, 5 & 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Wild et al (applicants' submission A6; Gene 1998, Vol. 223, pages 55-66; see the entire document). **This is a new rejection.**

Wild et al teach the retrofitting of pre-existing libraries of transposon insertions with FRT and oriV elements in order to use the retrofitted constructs for generation of large quantities of genomic DNA fragments (e.g. the Abstract). In Figure 7, Wild et al demonstrate the generation of isolated DNAs comprising recombination sequences in the order of Lox-FRT-Lox-FRT where the Lox sequences are in opposite orientation with one another and the FRT sequences are in opposite orientation with one another (e.g. Figure 7A). In this example the Lox sequences flank, at least, the first FRT sequence, and the FRT sequences flank the second Lox sequence as well as genomic sequences.

It appears that the Lox-FRT-Lox cassette present in the pMS10.1 (or pC1) and pMS10.2 (or pC2) vectors used to generate the recombinant molecules described in Figure 7 comprise additional sequences between the two Lox sites and the FRT site (e.g. see Figure 3; sequences include, at least, oriV, MCS2 and a BamHI restriction site). Further, it appears from both Figures 1 & 3 that there are multiple polynucleotides located between the adjacent loxP sequence and FRT sequence. For example, Figure 1a schematically depicts pC1 has having a gap between the FRT and LoxP sequence. Figure 3 shows at least a portion of a BamHI sequence located between the two different recombination sites. All that is needed for the teachings of Wild et al

to meet the limitation recited in amended claim 1 is a minimum of a trinucleotide sequence between the FRT and LoxP sequence (e.g. the sequence G-C-T comprises two distinct sequences, G-C and C-T).

Wild et al teach the construction of pC1 and pC2 in Section 2.4.2 on page 59. The authors do not explicitly teach that the adjacent FRT and LoxP sequence are separated by any particular number of polynucleotides. Yet, given the description of pC1 & pC2 in Figures 1 & 3 and the minimal number of nucleotides required to be present between the adjacent FRT and LoxP sites in these plasmids in order to read on the rejected claims, it is reasonable for the skilled artisan to expect that the product shown in Figure 7A (and present in the isolated nucleic acids run on the gels of Figure 7B & 7C) necessarily reads on the rejected claims.

Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Response to Arguments

Applicant's arguments filed in the response of 10/28/2004 to similar grounds of rejection have been fully considered but they are not persuasive. The response essentially argues that Wild et al do not teach the limitation incorporated into the amended claim (i.e. Wild et al teach that the FRT sequences flank the second Lox sequence). For the reasons indicated above, the examiner

has determined that a valid inherency argument can be made and has applied the new grounds of rejected recited above.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 54 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection necessitated by applicants' amendment filed on 10/28/2004. This is a New Matter rejection.**

Claim 54 has been amended to recite in step (iv) that the DNA molecule comprising the sequence 5'-L1-L2-sequence A-sequence B-L1-L2-3' further comprise additional site specific recombinase targeting sequences (L3) flanking the 5'-L1-L2-sequence A-sequence B-L1-L2-3' sequence and where the L3 sequence cannot recombine with L1 or L2. The response does not indicate where in the originally filed claims or specification support lies for the limitations recited in step (iv) of claim 54. The examiner has not been able to find literal support in the originally filed specification or claims for this amendment. Therefore, the newly added limitations in step (iv) of claim 54 are impermissible New Matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 5, 17, 19-21 & 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These are new rejections.**

Claim 5 is vague and indefinite in that the metes and bounds of the phrase "wherein sequences A and B are in a direction opposite to each other" are unclear. It is unclear how one determines if sequences A and B are in an orientation opposite to one another if they are not transcribed (as is specifically contemplated in claim 15). Does this limitation necessarily mean then that sequences A and B are each transcribed? Or is there some other means of determining if two 5'-3'sequences are oriented in a direction opposite to one another?

Claim 17 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "said protein" in claim 16, upon which claim 17 is dependent. Claim 16 recites, "wherein said translated sequences code for at least one protein" (examiner's emphasis). It is not clear, for example, whether the limitation recited in claim 17 (i.e. "said protein" is a protein of interest) *necessarily* applies to each protein when sequences A & B encode more than one protein.

Claim 19 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "said exon" in claim 18, upon which claim 19 is dependent. Claim 18 recites, "wherein sequences A and/or B encode at least one exon" (examiner's emphasis). It is not clear, for example, whether the limitation recited in claim 19 (i.e. differing from a "wildtype" exon) *necessarily* applies to each exon when sequences A & B encode more than one exon.

Claim 19 is further vague and indefinite in that the metes and bounds of the phrase "wherein said exon differs from the wild type exon of a protein of interest" are unclear. It is unclear what is intended for the term "the wild type exon" with regard to a protein of interest, particularly when multiple alleles for a given exon are possible in nature.

Claim 20 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "said protein" in claim 16, upon which claim 20 is dependent. Claim 16 recites, "wherein said translated sequences code for at least one protein" (examiner's emphasis). It is not clear, for example, whether the limitation recited in claim 20 (i.e. "said protein" is a is encoded by a cDNA) *necessarily* applies to each protein when sequences A & B encode more than one protein.

Claim 21 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "said reporter protein".

Claim 53 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "said protein" in claim 16, upon which claim 53 is dependent. Claim 16 recites, "wherein said translated sequences code for at least one protein" (examiner's emphasis). It is not clear, for example, whether the limitation recited in claim 17 (i.e. "said protein" is a reporter or selectable marker) *necessarily* applies to each protein when sequences A & B encode more than one protein.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101, which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v.*

Eagle Mfg. Co., 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 1 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 3 of copending Application No. 10/475,962. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

This rejection is based upon the claims pending in 10/457,962 as of the 1/27/2004 amendment of the claims in that application. Claim 3 of the '962 depends from claim 1 of the application and thus comprises all of the same limitations as are recited in claim 1.

The rejected claim and the claim of the '962 patent are not word-for-word identical to one another, but encompass the identical scope of nucleic acids. Each claim is directed to an isolated DNA molecule comprising at least a sequence A flanked by at least site specific recombinase targeting sequences (SSRTS) L1, and at least a sequence B flanked by at least site specific recombinase targeting sequences (SSRTS) L2, said L1 and L2 being unable to recombine with one another, wherein:

(i) sequences L1 are oriented in an opposite orientation to one another (e.g. convergent or divergent orientations),

(ii) sequences L2 are oriented in an opposite orientation to one another (e.g. convergent or divergent orientations),

(iii) the order of the SSRTS sequences in the DNA molecule are 5'-L1-L2-sequenceA-sequence B-L1-L2-3'.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 5-6, 8-13, 15-24 & 53 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 5-6, 8-11, 13 & 15-24 of copending Application No. 10/475,962. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. **This is a new rejection.**

As indicated above, claim 3 of the '962 application is identical in scope to instant claim 1. Each of the additional cited claims from the '962 application comprise the limitations recited in instant claims 5-6, 8-13, 15-24 & 53, but are not limited to the embodiment recited in claim 3 of the '962 application (i.e. they are dependent on claim 1 of the conflicting application). It would have been obvious to the skilled artisan to apply the particular limitations recited in claims 5-6, 8-11, 13 & 15-24 of the '962 application to the embodiment specifically recited in claim 3 because that embodiment is one of the 3 specifically recited embodiments encompassed by claim 1 of the application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. It is noted that, in the event of rejoinder of pending

methods claims with any allowed products claims for the instant application, new issues with regard to double patenting and the 10/475,962 application are likely to arise. As indicated above, the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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